REMARKS

Claims 1, 19, 22-24, and 30 have been canceled. Applicants reserve the right to pursue the subject matter of the canceled claims in related applications. Claims 40-41, 53, 73-74, and 87 have been amended to further specify that which Applicants regard as the invention. The amendments are fully supported by the specification and original claims and do not introduce any new matter.

Claims 31-107 will be pending upon entry of these amendments. Claims 98-107 are allowed. Claims 32, 33, 36-37, 54, and 58 are indicated as allowable if rewritten in independent form with all the limitations of the base claim and any intervening claims.

Formal Matters

The Examiner has made final Applicants' election of Group III, drawn to antibodies and corresponding to claims 22, 31-50, 53-83, and 87-107. However, claims 51-52 and 84-86 of Group VII, drawn to methods of using the antibodies of Group III, have been withdrawn from consideration. Since the claims of Groups III and VII are related as between a product and a process for using the product, and the process claims include all the limitations of the product, the Examiner in any case would be obligated to rejoin the method claims if the elected product claims are found allowable. In light of the decisions in *In re Ochiai*, 71 F.3d 1565, 37 USPQ2d 1127 (Fed. Cir. 1995) and *In re Brouwer*, 77 F.3d 422, 37 USPQ 2d 1663 (Fed. Cir. 1996), a notice was published in the Official Gazette which set forth new guidelines for the treatment of product and process claims. *See* 1184 OG 86 (March 26, 1996). Specifically, the notice states that "in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim depends from or otherwise includes all the limitations of an allowed product claim." *Id.* Accordingly, Applicants respectfully request that

if any of the claims of Group III are found allowable, the process claims of Group VII be rejoined and examined for patentability.

The title of the invention is objected to as not descriptive. See Paper No. 8 at page 3, paragraphs numbered 6 and 8. The title has been amended herein to reflect the claims under examination. Therefore, the withdrawal of this objection is respectfully requested.

The abstract is also objected to because it "does not reflect on the subject being claimed, which is the antibodies to the ICE-LAP3 and ICE-LAP4." *See* Paper No. 8 at page 3, paragraph numbered 6. Applicants disagree and traverse this objection. According to M.P.E.P. 608.01(b), "[a] patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains." M.P.E.P. 600-63, right column, second paragraph, emphasis added. The Guidelines For The Presentation of Patent Abstracts in M.P.E.P. 608.01(b) do not reveal any requirement that the patent abstract should reflect the *claims* pursued in a given application. To the contrary, the patent abstract is intended to reflect the patent *disclosure*. Applicants believe that the existing abstract is a fair reflection of Applicants' disclosure and thus no amendment is required. Withdrawal of this objection is respectfully requested.

The Examiner has stated that copies of the references listed as AA-CH on the form PTO/SB/08 submitted by Applicants on October 28, 2002 are not available and should be supplied again by Applicants. Applicants previously provided copies of these references for the parent application. The Examiner also states that these references have been "crossed out because none of the references have been submitted to the Office." Paper No. 8 at page 3, paragraph numbered 6. However, references AA-CH are not crossed out on the copy of the SB/08 returned to Applicants with Paper No. 8, but instead are initialed by the Examiner, indicating that they have been considered. Applicants request further clarification of whether

these references in fact have been considered and whether or not the copies previously submitted by Applicants are available to the Examiner.

Claim 22 is objected to as depending from claim 19, which is directed to a non-elected invention. Claim 22 also has been rejected under 35 U.S.C. 101 as directed to non-statutory subject matter for allegedly reading on antibodies found in nature. Claim 22 has been canceled, thereby obviating both the objection and the rejection.

The Rejection of Claims 64-83 and 87-97 Under 35 U.S.C. 112 for Enablement

Claims 64-83 and 87-97 stand rejected for alleged lack of enablement. Applicants are required to guarantee availability of ATCC Deposit Nos. 75873 and 75875 in order to enable the subject claims. A statement by an attorney of record confirming the availability of the deposited cDNA is attached to this paper. Thus, in light of that statement, withdrawal of the rejection is respectfully requested.

The Rejection of Claims 22, 31, 34-35, 38-39, 42-50, 53, 55-57, 59-83, and 87-97 Under 35 U.S.C. 112 for Enablement

Claims 22, 31, 34-35, 38-39, 42-50, 53, 55-57, 59-83, and 87-97 stand rejected for alleged lack of enablement over their full scope. The rejection is respectfully traversed.

Initially, claim 22 is rejected for alleged lack of enablement of antibodies against analogs or derivatives of polypeptides having the deduced amino acid sequence of Figure 1 or Figure 2 or of polypeptides encoded by the cDNA deposited in ATCC Deposit No. 75875 or 75873. However, since claim 22 has been canceled, the rejection is moot with respect to claim 22.

The remaining claims of this set are rejected because they allegedly recite "comprising" in such a way that the claims are "open-ended." The Examiner states:

> As to claims 31(c) through (h), claims 34-35, 38-39, 53(b) and (f), 55, 59, 64(c) through (d) and (g) through (h), 67-68, and 71-72, the term 'comprising' is open-ended. It expands the 30 or 50 contiguous amino acid residues of SEQ ID NO:2, SEQ ID NO:4, or cDNAs contained in ATCC Deposit Number 75875, or 75873 to include additional amino acid residues at either or both ends. There is insufficient guidance as to what types of amino acid residues can be added to either end and whether the resulting polypeptide would maintain both structure and function as protein of SEQ ID NO:2, SEQ ID NO:4 or the polypeptides encoded by the cDNAs contained in ATCC Deposit Number 75875 or 75873."

Paper No. 8 at page 9, lines 22-25. The Examiner appears to believe that the subject claims read on antibodies which bind to epitopes derived from amino acid sequences which are not described in the specification.

> Given the lack of guidance and working examples, predicting what changes can be made to the amino acid sequence mentioned above that after insertion and/or modification will retain both structure and have similar function as SEQ ID NO:2, SEQ ID NO:4, or the polypeptide encoded by the cDNAs contained in ATCC Deposit Number 75875 or 75873 is unpredictable."

Paper No. 8 at page 9, last line, through page 10, line 4. Applicants disagree with the Examiner's reading of the subject claims.

Claims 31-50 and 64-83 are directed to antibodies which specifically bind polypeptides whose sequences "consist of" portions of SEQ ID NO:2, SEQ ID NO:4, or the deposited cDNAs, even though some of these claims contain the word "comprises." For example, claim 31 part (c) recites "a protein consisting of a portion of SEQ ID NO:2, wherein said portion comprises at least 30 contiguous amino acid residues of SEQ ID NO:2." Even though the claim uses the word "comprises" to specify the portion of SEQ ID NO:2, the recited protein nevertheless consists of a portion of SEQ ID NO:2. Thus, since the antibodies of claims 31-50 and 64-83 specifically bind to amino acid sequences disclosed in the specification or encoded by the deposited cDNA clones, these claims are enabled as to their full scope.

Claims 53-63 and 87-97 recite antibodies obtained by immunizing an animal with a protein comprising a specified amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, or the

deposited cDNAs. For each of these claims, the binding specificity of the antibody is provided by the clause "wherein said antibody or fragment thereof specifically binds to said amino acid sequence." Emphasis added. Applicants have amended claims 53 and 87 to specify with even greater clarity that the recited amino acid sequences to which the antibody specifically binds are derived from SEQ ID NO:2, SEQ ID NO:4, or the deposited cDNAs. Like the previous group of claims, claims 53-63 and 87-97 recite antibodies that specifically bind to amino acid sequences disclosed in the specification or encoded by the deposited cDNA clones. Thus, claims 53-63 and 87-97 are also enabled over their full scope.

Claims 49-50 and 82-83 are directed to an isolated cell or a hybridoma that produces an antibody or fragment of an antibody. The Examiner states that these claims are not enabled because "it is well known that cell line and hybridoma produce the whole antibody and not the antibody fragment." Paper No. 8 at page 10, lines 21-22. Applicants disagree. With respect to an isolated cell, it is clear that one of skill in the art would know, based on the teachings in the specification and the general knowledge in the art, how to engineer a cell to produce a fragment of the antibody of claim 31 or of claim 64. Whether a cell produces the whole antibody or a fragment of the antibody is merely a question of which coding sequences the cell is engineered with. Hybridomas can also produce either an entire antibody or a fragment of an antibody. For example, the results shown in Fig. 2 of Ochi et al. (Proc. Natl. Acad. Sci. USA 80:6351-6355 (1983), attached as Exhibit A) point out that a hybridoma cell line can give rise to subclones which lack various portions of an immunoglobulin molecule. Thus, claims 49-50 and 82-83 are also enabled as to their entire scope.

For the reasons discussed above, the withdrawal of this rejection is respectfully requested.

The Rejection of Claims 22, 31, 34-35, 38-39, 42-50, 53, 55-57, 59-83, and 87-97 Under 35 U.S.C. 112 for Written Description

Claims 22, 31, 34-35, 38-39, 42-50, 53, 55-57, 59-83, and 87-97 stand rejected for alleged lack of written description. The rejection is respectfully traversed.

Initially, Applicants point out that the cancellation of claim 22 has obviated the rejection with respect to that claim.

This rejection is based on the same reasoning as the previous rejection for alleged lack of enablement. The Examiner states:

> [T]here is inadequate written description about the structure associated with functions of any protein 'comprising' the amino acid sequence of at least 30 or 50 contiguous amino acid residues of SEQ ID NO:2 or SEQ ID NO:4 or polypeptide encoded by the encoded by the [sic] cDNAs contained in ATCC Deposit Number 75875, and 75873. The phrase 'comprising' is open-ended. It expands the 30 or 50 contiguous amino acid residues of SEQ ID NO:2, SEQ ID NO:4 or polypeptides encoded by cDNAs contained in ATCC Deposit Number 75875, and 75873 to include additional amino acid residues at either or both ends. Given the indefinite number of undisclosed amino acids that can be added, there is inadequate written description about the undisclosed amino acids, let alone the protein having the same functions.

Paper No. 8 at page 13, lines 6-15. For the same reasons discussed above for the enablement rejection, Applicants respectfully point out that the amino acid sequences which specifically bind to the claimed antibodies are fully disclosed in the specification. The claimed antibodies bind to sequences disclosed in SEQ ID NO:2, SEQ ID NO:4, or encoded by the cDNAs of ATCC Deposit Number 75875 or 75873. Therefore, the withdrawal of this rejection is respectfully requested.

The Rejection of Claims 40-41, 46, 73-74, and 79 Under 35 U.S.C. 112, Second Paragraph

Claims 40-41 and 73-74 stand rejected as allegedly indefinite for lack of antecedent basis. Claims 46 and 79 allegedly fail to further limit the claims from which they depend. Applicants respectfully traverse the rejection.

The Examiner states that in claim 40 there is no antecedent basis for "protein (b)" in base claim 32. Similar antecedent basis problems allegedly are found in claims 41, 73, and 74. Claims 40-41 and 73-74 have been amended to more clearly specify the antecedent basis for "protein (b)" in claim 40 and similar expressions in claims 41, 73, and 74. Applicants submit that the amended claims are not indefinite and respectfully request withdrawal of the rejection.

Claims 46 and 79 recite the antibodies of claims 31 and 64, respectively, which are labeled. Because not all of the antibodies of either claim 31 or claim 64 are labeled, Applicants submit that claims 46 and 79 do in fact further limit their respective base claims and are proper. Withdrawal of the rejection is respectfully requested.

The Rejection of Claims 22, 31, 34-35, 38-39, 43-44, and 48-50 under 35 U.S.C. 102(e)

Claims 22, 31, 34-35, 38-39, 43-44, and 48-50 stand rejected as allegedly anticipated under 35 U.S.C. 102(e) by U.S. Patent 5,552,536. The rejection is respectfully traversed.

Initially, Applicants point out that the cancellation of claim 22 has obviated the rejection with respect to that claim.

The '536 patent discloses an ICE-related cysteine protease III (ICE REL-III) which bears the QACRG consensus pentapeptide sequence shared by ICE-related cysteine proteases. This consensus sequence was identified in the instant specification at page 2 and again at page 5, where its presence in ICE-LAP-3 at amino acid residues 259-263 and in ICE-LAP-4 at residues 161-165 is acknowledged. The '536 patent teaches generally making antibodies to ICE REL-III

or fragments thereof, but does not teach any particular antigenic epitopes or any actual antibodies.

Regarding alleged anticipation of the subject claims by the '536 patent, the Examiner states:

> The term 'comprising' is open ended. It expands the claimed polypeptide fragment to include additional amino acid residues at either or both ends to read on the reference polypeptide. Thus, the reference teachings anticipate the claimed invention.

Paper No. 8 at page 15, lines 10-12. Applicants disagree. As discussed above for the enablement rejection, the claimed antibodies specifically bind to amino acid sequences from either SEQ ID NO:2, SEQ ID NO:4, or those encoded by the deposited cDNAs in ATCC Deposit No. 75875 or 75873. The claimed antibodies do not specifically bind to ICE REL-III because any extensions of the fragments recited in the subject claims are taken from the amino acid sequence of either SEQ ID NO:2, SEQ ID NO:4, or the amino acid sequence encoded by the deposited cDNA in ATCC Deposit No. 75875 or 75873. Furthermore, the subject claims require that the recited antibodies specifically bind to the recited ICE-LAP-3 or ICE-LAP-4 polypeptides. Even if an antibody can be made which binds to the QACRG consensus sequence alone, such an antibody would not fall within the subject claims because it would not be specific for ICE-LAP-3 or ICE-LAP-4 polypeptides. Thus, the subject claims do not read on the ICE REL-III polypeptide disclosed in the '536 patent. Withdrawal of the rejection is respectfully requested.

The Rejection of Claims 22, 31, 34-35, 38-39, 43-44, and 48 Under 35 U.S.C. 103 (a)

Claims 22, 31, 34-35, 38-39, 43-44, and 48 stand rejected as allegedly obvious over Cerretti et al. in view of Campbell et al. The rejection is respectfully traversed.

Initially, Applicants point out that the cancellation of claim 22 has obviated the rejection with respect to that claim.

Cerretti et al. teach interleukin-1ß converting enzyme (ICE), which has a QACRG pentapeptide sequence shared by ICE-LAP-3 at residues 259-263 and ICE-LAP-4 at residues 161-165. Applicants note that while Cerretti et al. teach an ICE-specific antiserum (*see, e.g.*, Fig. 2), they do not teach antibodies to fragments of ICE such as QACRG. Campbell et al. teach that "it is customary now for any group working on a macromolecule to both clone the gene encoding for it and make monoclonal antibodies to it (sometimes without a clear objective for their application)". Paper No. 8 at page 17, lines 16-18. The Examiner states that Campbell et al. teach generally the making of polyclonal and monoclonal antibodies and their use in an ELISA.

As before, the Examiner mistakenly interprets the subject claims as reading on antibodies that specifically bind undisclosed amino acid sequences fused to fragments of ICE-LAP-3 or ICE-LAP-4 polypeptides. "The term 'comprising' is open-ended. It expands the polypeptide to which the antibody binds to include additional amino acid residues at either or both ends to read on the reference polypeptide as taught by Cerretti et al.." Paper No. 8 at page 17, line 31 through page 18, line 1. Applicants disagree. The subject claims are directed to antibodies that specifically bind amino acid sequences of ICE-LAP-3 or ICE-LAP-4, *i.e.*, the fragments of SEQ ID NO:2, SEQ ID NO:4, or of the amino acid sequence encoded by the cDNA in ATCC Deposit No. 75875 or 75873, as recited in the subject claims. While the QACRG sequence is common to ICE, ICE-LAP-3, and ICE-4, any antibody that specifically binds only the QACRG pentapeptide sequence (if such exists) would not *specifically* bind the ICE-LAP-3 or ICE-LAP-4 sequences of the subject claims. On the other hand, any antibody that does not specifically bind to QACRG alone, but specifically binds an epitope of ICE-LAP-3 or ICE-LAP-4 which includes

QACRG, is not an antibody taught or suggested by Cerretti et al. Thus, Cerretti et al., either alone or combined with Campbell et al., does not teach or suggest all the characteristics of the antibodies of claim 31 or claims 34-35, 38-39, 43-44, and 48 which depend therefrom.

Withdrawal of the rejection is respectfully requested.

The Rejection of Claims 31 and 45 Under 35 U.S.C. 103 (a)

Claims 31 and 45 stand rejected as allegedly obvious over Cerretti et al. or U.S. Patent 5,552,536 in view of U.S. Patent 5,530,101. The rejection is respectfully traversed.

The teachings of Cerretti et al. and U.S. Patent 5,552,536 have been discussed above. U.S. Patent 5,530,101 teaches chimeric or humanized antibodies.

The combination of either Cerretti et al. or the '536 patent with the '101 patent fails to teach or suggest the antibodies of the instant claims for the same reasons discussed for the preceding rejection (for Cerretti) or for the 102(e) rejection (for the '536 patent). Neither combination of references teaches or suggests the recited amino acid sequences to which the antibodies specifically bind.

The withdrawal of the rejection is respectfully requested.

The Rejection of Claims 31, 43-44, and 49-50 Under 35 U.S.C. 103 (a)

Claims 31, 43-44, and 49-50 stand rejected as allegedly obvious over Cerretti et al. in view of Harlow et al. The rejection is respectfully traversed.

The teachings of Cerretti et al. have been discussed above. Harlow et al. teach methods of making polyclonal and monoclonal antibodies.

The combination of Cerretti et al. and Harlow et al. fails to teach or suggest the antibodies of the instant claims for the same reasons discussed above. The combination of

references fails to teach or suggest the recited amino acid sequences to which the antibodies specifically bind.

The withdrawal of the rejection is respectfully requested.

The Rejection of Claims 31 and 45-47 Under 35 U.S.C. 103 (a)

Claims 31 and 45-47 stand rejected as allegedly obvious over Cerretti et al. in view of Harlow et al. The rejection is respectfully traversed.

The teachings of Cerretti et al. have been discussed above. Harlow et al. teach Fab fragments and methods of labeling antibodies, including labeling with an enzyme.

The combination of Cerretti et al. and Harlow et al. fails to teach or suggest the antibodies of the instant claims for the same reasons discussed above. The combination of references fails to teach or suggest the recited amino acid sequences to which the antibodies specifically bind.

The withdrawal of the rejection is respectfully requested.

The Rejection of Claims 31 and 46-47 Under 35 U.S.C. 103 (a)

Claims 31 and 46-47 stand rejected as allegedly obvious over Cerretti et al. in view of Harlow et al. The rejection is respectfully traversed.

The teachings of Cerretti et al. have been discussed above. Harlow et al. teach methods of labeling antibodies, including labeling with an enzyme.

The combination of Cerretti et al. and Harlow et al. fails to teach or suggest the antibodies of the instant claims for the same reasons discussed above. The combination of references fails to teach or suggest the recited amino acid sequences to which the antibodies specifically bind.

The withdrawal of the rejection is respectfully requested.

The Rejection of Claims 31 and 45 Under 35 U.S.C. 103 (a)

Claims 31 and 45 stand rejected as allegedly obvious over Cerretti et al. or U.S. Patent 5,552,536 in view of U.S. Patent 5,260,203. The rejection is respectfully traversed.

The teachings of Cerretti et al. and U.S. Patent 5,552,536 have been discussed above. U.S. Patent 5,260,203 teaches making single chain antibodies.

The combination of either Cerretti et al. or the '536 patent with the '203 patent fails to teach or suggest the antibodies of the instant claims for the same reasons discussed above. Neither combination of references teaches or suggests the recited amino acid sequences to which the antibodies specifically bind.

The withdrawal of the rejection is respectfully requested.

Conclusion

Entry of the above amendment is respectfully solicited. In view of the foregoing remarks, Applicants believe that this application is now in condition for allowance, and an early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the examination of this application.

Finally, if there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the appropriate fee should also be charged to our Deposit Account.

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Respectfully submitted,

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